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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,657	03/03/2006	Robert M. Jones	34.US5.PCT	4098

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EXAMINER	
MURRAY, JEFFREY H	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
05/13/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/541,657	JONES ET AL.	
	Examiner	Art Unit	
	JEFFREY H. MURRAY	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,12-14,16-66,73,74,78-85,87-92 and 100* is/are pending in the application.

4a) Of the above claim(s) *4,5,62-66,79-85,87-92 and 100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-3,12-14,16-61,73,74 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 June 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to an amendment filed on March 17, 2010. There are seventy-six claims pending and fifty-five claims under consideration. Claims 1-3, 12-14, 16-61, 73, 74 and 78 are pending. Claims 6-11, 15, 67-72, 75-77, 86 and 93-99 have been cancelled. Claims 4, 5, 62-66, 79-85, 87-92 and 100 have been withdrawn. This is the third action on the merits.

Election/Restrictions

Applicants have stated that the examiner has not provided reasoning for the current restriction requirement as requested in the petition decision. The reasoning for the lack of unity of invention is the same as when the restriction requirement was originally filed. The technical feature linking the claims is a compound of general formula I. In the instant case, Groups I-XIII are directed to structurally dissimilar compounds such that the variable core created by varying the definitions of the Formula do not belong to a recognized class of chemical compounds in the art, and references that exist in anticipating one invention would not render obvious the others. For example, a 5-methyl-N-phenyl-6-(pyrrolidin-1-yl)pyrimidin-4-amine is different from a N-(2-cyclohexyl-5-(pyridin-4-yl)-6-(1,3,6-triazocan-1-yl)pyrimidin-4-yl)pyrimido[4,5-d]pyrimidin-4-amine. Thus, as before, separate searches in the literature would be required. The amending of the claims and removal of a few terms has not created unity of invention. Here, each group's compounds are made and used independently of each other and could support separate patents. The compounds differ significantly in chemical structures. One skilled in the art would not consider such diverse structures

as functional equivalents of each other. The mere fact that there is a single similarity is not in itself a significant reason to render the whole embodiment obvious. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants. Therefore the feature linking the claims does not constitute a special technical feature as defined by PCT Rule 13.2 as it does not define a contribution over the art.

Applicants have also argued that no mention was made of the lack of unity of invention specifically between the compounds and the methods of use. The 37 CFR 1.457(b) states:

> A national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are ***drawn only to one*** of the following combinations of categories: (emphasis added)
> (1) manufacture of said product; or
> (2)A product and process of use of said product; or
> (3)A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
> (4)A process and an apparatus or means specifically designed for carrying out the said process; or
> (5)A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process

It is clear that the applicants have more than one of these categories present. Applicants have in their application, the combination of various products, methods of producing a pharmaceutical composition and ***multiple*** processes of use of said product (ie. treatment of a metabolic disorder, modulating RUP3, controlling or decreasing weight gain, etc.) Accordingly, Groups I – XVII are not so linked by the same or a

corresponding special technical feature as to form a single general inventive concept. The restriction is deemed proper and once again made **FINAL**.

Withdrawn Rejections/Objections

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

Claim Objections

Claims 1-3, 12-14, 16-61, 73, 74 and 78 are objected to because of the following informalities:

Claims 1-3, 12-14, 16-61, 73, 74 and 78 are objected to for not containing proper Markush language. Examiner suggests rewriting the claims to read, "…or a pharmaceutically acceptable salt,…" so as to be in the proper alternative format within the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 12-14, 16-61, 73, 74 and 78 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutically acceptable salt, does not reasonably provide enablement for any hydrates or solvates within the broad Claim 1. The specification does not enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicants first argue that the response was based on an entirely different application. This is false. While typographical errors were noted in a previous response, the examiner points the applicants to the first paragraph of the previous response, which pinpoints a specific argument. The paragraph is seen below:

> Claims 1-3, 9, 11-61, 70, 72-76 and 78 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pyrimidine where R_1 is a hydrogen; the N-A-B-D ring is a piperidinyl ring; and Ar_1 is a phenyl, benzyl, fused phenyl or fused benzyl ring, does not reasonably provide enablement for all of the other groups listed nor any hydrates or solvates within the broad Claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

It is clearly seen here that the argument refers to "…a pyrimidine where R_1 is hydrogen; the N-A-B-D ring is a piperidinyl ring; and Ar_1 is a phenyl, benzyl, fused phenyl or fused benzyl ring…" Examiner notes that the previously written argument that applicant has referred to, contains no structures such as an N-A-B-D ring.

Applicants then refer to a separate application and note that approximately 1-2 pages of the 15 page response appear to be almost identical in terms of text. Applicants argue since one application deals with triazolopyrimidines and pyrazolopyrimidines while the current application deals with pyrimidines that the specification may not have even been considered. What applicant does not point out is that the pages in question both are arguing the same point in two separate applications,

that of a solvate and/or hydrate being non-enabled. Hence the same literature references (Dorwald, et. al. and Vippagunta, et. al.) are quoted. These two literature quotations comprise of the majority of the “identical text" applicant has pointed out. Examiner assures the applicants that their specification was given *bona fide* consideration during the enablement rejection

Applicants have argued that solvates and hydrates have been reasonably enabled, examiner disagrees. Applicants continue to point to the first line in section 3.1 of Vippagunta, et. al. which states that one third of pharmaceutical compounds are capable of forming crystalline hydrates. The mere capability of something does not make it enabled in the current application.

The test for enablement is whether any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. See MPEP 2164.01.

The applicants have cited that over **300 compounds** have been provided in this application along with over 200 pages showing that a “tremendous amount of guidance” has been provided. In regards to the compounds themselves examiner agrees guidance has been provided. However, examiner has pointed out in past actions that while the applicants have provided details on how to make the compounds, and cited over 300 examples, that is irrelevant to the specifics of the current argument. The argument stated here is whether the application is enabled for making/using hydrates

and solvates of these compounds. In this regard, the application has provided **zero compounds** which are exemplary representatives of any hydrates or solvates. In addition, the specification has not provided any details as to how to make either specific hydrates or solvates of these compounds or to make hydrates or solvates generally.

The applicants have also argued that the Vippagunta reference focuses on "predicting the structure and stability of solvates, which does not weigh heavily against the enablement of the present claims since the claims do not recite solvates of particular structure of stability." However, Vippagunta also discusses not only the structure and stability of hydrates, but also their formation in general. Page 18 of the reference states:

> "*Predicting the formation of solvates or hydrates of a compound...is complex and difficult*. Each solid compound responds uniquely to the possible formation of solvates or hydrates and *hence generalizations cannot be made for a series of related compounds*." (emphasis added.)

This statement, tells one skilled in the art that 1) the formation of a solvate or hydrate is complex and difficult; and, 2) they cannot presume that if one compound in a series of related compounds forms a hydrate or solvate that any or all of the remaining related compounds can or will form a solvate or hydrate." Thus applicants attempt to point out pyrimidine hydrates known in the prior art is meaningless. Vippagunta clearly states that generalizations cannot be made for a series of related compounds.

Applicants argue in addition that "…even if solvate formation were somewhat unpredictable, as the examiner contends, the claims would still satisfy the enablement requirement because such experimentation…would be routine and well within the

capacity of the skilled artisan, and therefore would not be undue." The examiner is not contending that solvate and hydrate formation is "somewhat unpredictable" rather the examiner is merely restating exactly what the Vippagunta reference states, that "*Predicting the formation of solvates or hydrates of a compound…is complex and difficult*." In a previous action, examiner stated that Vippagunta points out approximately two thirds of all pharmaceutical compounds are *incapable* of forming solvates or hydrates. For all of these compounds, the experimentation would not only be "undue" but the experimentation would fail. The literature shows that only one third of all pharmaceutical compounds are even capable of forming a hydrate or solvate. Of these, predicting the formation of them is complex and difficult and compounds in a related series can not be predicted to act similarly.

The test for enablement has not been met. While the claims do support pyrimidine compounds and their pharmaceutically acceptable salts, they do not support the hydrates or solvates of these compounds. The disclosure does not contain sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use solvates or hydrates of the claimed compounds. No new matter permitted. Appropriate correction is required.

Conclusion

Claims 1-3, 12-14, 16-61, 73, 74 and 78 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is 571-272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisors, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey H Murray/
Patent Examiner , Art Unit 1624

/James O. Wilson/
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